

We claim:

5 1. A reagent comprising:
a coagulation activator capable of allowing assessment of the
hemostatic potential of a blood or plasma sample.

10 2. The reagent of claim 1, further comprising vesicles or liposomes.

15 3. The reagent of claim 1, wherein the coagulation activator
comprises tissue factor.

20 4. The reagent of claim 3, further comprising a metal cation or metal
salt which dissociates into a metal cation.

25 5. The reagent of claim 1, wherein the reagent is capable of indicating
a sample to be any of hypocoagulable, normal or hypercoagulable,
depending upon the condition of the patient from which the sample
was taken.

30 6. The reagent of claim 1, wherein the reagent is capable of indicating
a patient, from which the sample was taken, to have any of
thrombotic tendency, hemorrhagic tendency, or stasis, depending
on the patient.

7. The reagent of claim 2, wherein the vesicles comprise
phospholipids.

8. The reagent of claim 7, wherein the phospholipids comprise one or
more of phosphatidylcholine, phosphatidylethanolamine and
phosphatidylserine.

30 9. The reagent of claim 8, wherein the phospholipid mixture comprise
all of phosphatidylcholine, phosphatidylethanolamine and

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phosphatidylserine and at a ratio of approximately from 1 to 10 mole percent phosphatidylserine and from about 5 to 30 mole percent phosphatidylethanolamine and the remainder phosphatidylcholine.

10. The reagent of claim 9 wherein the phospholipid mixture comprises approximately 70 mole percent phosphatidylcholine, 20 mole percent phosphatidylethanolamine and 10 mole percent phosphatidylserine.

11. The reagent of claim 3, wherein the tissue factor comprises recombinant or purified tissue factor, truncated tissue factor, or cells expressing tissue factor on their surface.

12. The reagent of claim 4, wherein the metal cation is a divalent metal cation selected from magnesium, calcium or manganese.

13. The reagent of claim 4, wherein the metal salt is a halide of magnesium, calcium or manganese.

14. The reagent of claim 1, further comprising an activator of an anticoagulant pathway.

15. The reagent of claim 14, wherein the activator of the anticoagulant pathway is an activator of protein C.

16. The reagent of claim 15, wherein the protein C activator is purified human thrombomodulin, purified non-human mammalian thrombomodulin, soluble or membrane associated thrombomodulin, native thrombomodulin or thrombomodulin reconstituted with phospholipids, partially or fully glycosylated thrombomodulin, fully deglycosylated thrombomodulin.

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17. The reagent of claim 1, further comprising buffers and/or stabilizers.

5 18. The reagent of claim 11, wherein the tissue factor is at a concentration of 11 picomolars or less.

19. The reagent of claim 18, wherein the tissue factor is at a concentration of 6 picomolars or less.

10 20. The reagent of claim 19, wherein the tissue factor is at a concentration of 3 picomolars or less.

21. The reagent of claim 1, further comprising phospholipids at a concentration of from 10 to 300 micromolar.

15 22. The reagent of claim 21, wherein the phospholipids are at a concentration of from 50 to 200 micromolar.

23. The reagent of claim 15, wherein the protein C activator is thrombomodulin at a concentration of 30 nanomolar or less.

20 24. The reagent of claim 23, wherein the thrombomodulin is at a concentration of from 5 to 20 nanomolar.

25 25. The reagent of claim 13, wherein the metal salt is at a concentration of from 5 to 50 mM.

26. The reagent of claim 25, wherein the metal salt is at a concentration of from 15 to 35 mM.

30 27. A reagent comprising:
a coagulation activator at a concentration of 11 picomolar or less.

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5 28. The reagent of claim 27, further comprising vesicles or liposomes.

10 29. The reagent of claim 27, wherein the coagulation activator comprises tissue factor at a concentration of 11 picomolar or less.

15 30. The reagent of claim 29, further comprising a metal cation or metal salt which dissociates into a metal cation.

20 31. The reagent of claim 27, wherein the reagent is capable of indicating a sample to be any of hypocoagulable, normal or hypercoagulable, depending upon the condition of the patient from which the sample was taken.

25 32. The reagent of claim 27, wherein the reagent is capable of indicating a patient, from which the sample was taken, to have any of thrombotic tendency, hemorrhagic tendency, or stasis, depending on the patient.

30 33. The reagent of claim 28, wherein the vesicles comprise phospholipids.

34. The reagent of claim 33, wherein the phospholipids comprise one or more of phosphatidylcholine, phosphatidylethanolamine and phosphatidylserine.

35. The reagent of claim 34, wherein the phospholipid mixture comprise all of phosphatidylcholine, phosphatidylethanolamine and phosphatidylserine and at a ratio of approximately from 0 to 10 mole percent phosphatidylserine and from about 5 to 30 mole percent phosphatidylethanolamine and the remainder phosphatidylcholine.

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36. The reagent of claim 29, wherein the tissue factor comprises recombinant or purified tissue factor, truncated tissue factor, or cells expressing tissue factor on their surface.

5 37. The reagent of claim 30, wherein the metal cation is a divalent metal cation selected from magnesium, calcium or manganese.

38. The reagent of claim 30, wherein the metal salt is a halide of magnesium, calcium or manganese.

10 39. The reagent of claim 27, further comprising an activator of an anticoagulant pathway.

40. The reagent of claim 39, wherein the activator of the anticoagulant pathway is an activator of protein C.

15 41. The reagent of claim 40, wherein the protein C activator is purified human thrombomodulin, purified non-human mammalian thrombomodulin, soluble or membrane associated thrombomodulin, native thrombomodulin or thrombomodulin reconstituted with phospholipids, partially or fully glycosylated thrombomodulin, or fully deglycosylated thrombomodulin.

20 42. The reagent of claim 27, further comprising buffers and/or stabilizers.

25 43. The reagent of claim 36, wherein the tissue factor is at a concentration of 8 picomolars or less.

30 44. The reagent of claim 43, wherein the tissue factor is at a concentration of 6 picomolars or less.

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45. The reagent of claim 44, wherein the tissue factor is at a concentration of 3 picomolars or less.

5 46. The reagent of claim 27, further comprising phospholipids at a concentration of from 10 to 300 micromolar.

47. The reagent of claim 46, wherein the phospholipids are at a concentration of from 50 to 200 micromolar.

10 48. The reagent of claim 40, wherein the protein C activator is thrombomodulin at a concentration of 30 nanomolars or less.

49. The reagent of claim 48, wherein the thrombomodulin is at a concentration of from 5 to 15 nanomolar.

15 50. The reagent of claim 38, wherein the metal salt is at a concentration of from 5 to 50 mM.

51. The reagent of claim 50, wherein the metal salt is at a concentration of from 15 to 35 mM.

20 52. A kit for assessing the hemostatic potential of a test sample comprising:
a coagulation activator at a concentration of 11 picomolar or less, or a coagulation activator and instructions for diluting the coagulation activator to a concentration of 11 picomolar or less;
vesicles;
a metal divalent cation or a metal salt capable of dissociating into a metal divalent cation;
instructions for adding the coagulation activator, metal cation or metal salt, and vesicles to a test sample, and instructions for assessing the hemostatic potential of the test sample.

53. The kit of claim 52, wherein the vesicles are a plurality of different phospholipids.

54. The kit of claim 52, wherein the coagulation activator comprises tissue factor at a concentration of 11 picomolar or less.

55. The kit of claim 54, further comprising a calcium cation or calcium salt that dissociates into a calcium cation.

10 56. The kit of claim 52, wherein the kit is capable of indicating a sample to be any of hypocoagulable, normal or hypercoagulable, depending upon the condition of the patient from which the sample was taken.

15 57. The kit of claim 52, wherein the kit is capable of indicating a patient, from which the sample was taken, to have any of thrombotic tendency, hemorrhagic tendency, or stasis, depending on the patient.

20 58. The kit of claim 53, wherein the vesicles comprise platelets or phospholipids.

25 59. The kit of claim 58, wherein the phospholipids comprise one or more of phosphatidylcholine, phosphatidylethanolamine and phosphatidylserine.

30 60. The kit of claim 59, wherein the phospholipids comprise all of phosphatidylcholine, phosphatidylethanolamine and phosphatidylserine and at a ratio of approximately from 0 to 10 mole percent phosphatidylserine and from about 5 to 30 mole percent phosphatidylethanolamine and the remainder phosphatidylcholine.

61. The kit of claim 60 wherein the phospholipid mixture comprises approximately 70 mole percent phosphatidylcholine, 20 mole percent phosphatidylethanolamine and 10 mole percent phosphatidylserine.

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62. The kit of claim 54, wherein the tissue factor comprises recombinant or purified tissue factor, truncated tissue factor, or cells expressing tissue factor on their surface.

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63. The kit of claim 55, wherein the metal cation is a divalent metal cation selected from magnesium, calcium or manganese.

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64. The kit of claim 55, wherein the metal salt is a halide of magnesium, calcium or manganese.

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65. The kit of claim 52, further comprising an activator of an anticoagulant pathway and instruction for adding the activator to the test sample.

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66. The kit of claim 65, wherein the activator of the anticoagulant pathway is an activator of protein C.

67. The kit of claim 66, wherein the protein C activator is purified human thrombomodulin, purified non-human mammalian thrombomodulin, soluble or membrane associated thrombomodulin, native thrombomodulin or thrombomodulin reconstituted with phospholipids, partially or fully glycosylated thrombomodulin, or fully deglycosylated thrombomodulin.

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68. The kit of claim 52, further comprising buffers and/or stabilizers.

69. The kit of claim 62, wherein the tissue factor is at a concentration of 8 picomolars or less.

70. The kit of claim 69, wherein the tissue factor is at a concentration of 6 picomolars or less.

5 71. The kit of claim 70, wherein the tissue factor is at a concentration of 3 picomolars or less.

72. The kit of claim 52, further comprising phospholipids at a concentration of from 10 to 300 micromolar.

10 73. The kit of claim 72, wherein the phospholipids are at a concentration of from 50 to 200 micromolar.

74. The kit of claim 66, wherein the protein C activator is thrombomodulin at a concentration of 30 nanomolar or less.

15 75. The kit of claim 74, wherein the thrombomodulin is at a concentration of from 5 to 20 nanomolar.

76. The kit of claim 64, wherein the metal salt is at a concentration of from 5 to 50 mM.

20 77. The kit of claim 76, wherein the metal salt is at a concentration of from 15 to 35 mM.

78. The kit of claim 74, wherein the thrombomodulin is provided separately from the coagulation activator.

25 79. The kit of claim 78, wherein the thrombomodulin is provided mixed with heparin, heparin sulphate or heparin-like molecules.

80. The kit of claim 52, wherein the coagulation activator is provided mixed with vesicles, the metal ions or metal salt are provided

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separately from the coagulation activator, and an activator of an anticoagulation pathway is provided separately from the metal ions or salt, and separately from the coagulation activator.

5 81. The kit of claim 80, wherein in a first container is provided tissue factor at a concentration of 11 picomolars or less mixed with vesicles which are phospholipids at a concentration of from 10 to 300 picomolar, in a second container is provided a metal salt in a concentration of from 5 to 50 mM, and in a third container is provided the coagulation activator which is thrombomodulin at a concentration of 30 nanomolar or less.

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15 82. The kit of claim 52, wherein a first container is provided having the coagulation activator which is tissue factor at a concentration of 11 picomolar or less mixed with vesicles which are phospholipids at a concentration of from 10 to 300 picomolar, a second container is provided having a metal salt in a concentration of from 5 to 50 micromolar, and a third container having the coagulation activator which is tissue factor at a concentration of 11 picomolar or less mixed with vesicles which are phospholipids at a concentration of from 10 to 300 picomolar and an activator of an anticoagulant pathway which is thrombomodulin at a concentration of 30 nanomolar or less.

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25 83. The reagent of claim 16, wherein the thrombomodulin comprises heparin or heparin-like molecules.

84. The reagent of claim 16, wherein the thrombomodulin is relipidated with phospholipids comprising at least 10% phosphatidylethanolamine.

30 85. The reagent of claim 2, wherein the vesicles comprise platelets, cellular debris, phospholipid vesicles or platelet microparticles.

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86. The reagent of claim 2, wherein the vesicles are phospholipid vesicles prepared by dilution, sonication, dialysis or extrusion.

87. The reagent of claim 1, wherein the coagulation activator comprises tissue factor-rich mammalian tissue extracts, tissue factor purified from mammalian tissues or thromboplastin.

88. The reagent of claim 1, wherein the coagulation activator is capable of detecting defects in the initiation phase.

89. The reagent of claim 41, wherein the thrombomodulin comprises heparin or heparin-like molecules.

90. The reagent of claim 41, wherein the thrombomodulin is relipidated with phospholipids comprising at least 10% phosphotidylethanolamine.

91. The reagent of claim 28, wherein the vesicles comprise platelets, cellular debris, phospholipid vesicles or platelet microparticles.

92. The reagent of claim 28, wherein the vesicles are phospholipid vesicles prepared by dilution, sonication, dialysis or extrusion.

93. The reagent of claim 27, wherein the coagulation activator comprises tissue factor-rich mammalian tissue extracts, tissue factor purified from mammalian tissues or thromboplastin.

94. The reagent of claim 27, wherein the coagulation activator is capable of detecting defects in the initiation phase.

95. The kit of claim 67, wherein the thrombomodulin comprises heparin or heparin-like molecules.

96. The kit of claim 67, wherein the thrombomodulin is relipidated with phospholipids comprising at least 10% phosphatidylethanolamine.
97. The kit of claim 52, wherein the vesicles comprise platelets, cellular debris, phospholipid vesicles or platelet microparticles.
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98. The kit of claim 52, wherein the vesicles are phospholipid vesicles prepared by dilution, sonication, dialysis or extrusion.
- 10 99. The kit of claim 52, wherein the coagulation activator comprises tissue factor-rich mammalian tissue extracts, tissue factor purified from mammalian tissues or thromboplastin.
100. The kit of claim 52, wherein the coagulation activator is capable of
15 detecting defects in the initiation phase.